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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,188	12/21/2001	Charles S. Zuker	02307E-114910US	9521

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,188	ZUKER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,12 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-9, 12, 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/23/2006 has been entered. Applicant is reminded that the claims will be examined only to the extent that they read on the elected SEQ ID NO: 8, as set forth previously.

Response to Amendment

Applicant is notified that any outstanding rejection, or basis of an outstanding rejection, that is not explicitly maintained in this Office Action has been withdrawn in view of further consideration and/or Applicant's amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-9, 12, 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require methods of identifying a compound that modulates taste signaling (claim 1), or methods of modulating taste signaling (claim 12), by determining a functional effect

of the compound upon a cell of cell membrane, wherein the functional effect is under the influence of a taste-cell specific ion channel subunit (TC-ICS, see page 5 of the specification). During the prosecution of the instant application, the phrases and words "modulate", "functional effect", and "under the influence of" have been under question as to their impact on the claims with regard to making the claims indefinite. Upon further consideration of the art of ion channels, and including Applicant's arguments, the basis of the rejection regarding the word "modulates" is now removed.

Regarding "functional effect" the examiner previously withdrew that basis of the rejection because the claims had been amended to clarify what the functional effect was, i.e. "change in intracellular ion concentration, a change in transmembrane ion flux of an ion, or a change in intracellular Ca^{2+}". However this was erroneous for several reasons. The claims are open-ended with regard to what functional effect is to be identified, i.e. they recite "wherein the functional effect *comprises* a change in intracellular ion concentration, a change in transmembrane ion flux of an ion, or a change in intracellular Ca^{2+}". While it can be understood that a functional effect may include a particular recited effect and also many others, e.g. those involved in the signal transduction cascade, the claims do not set forth which functional effect is to be determined. When read in light of the specification, this could (or could not) include practically any functional effect that "indirectly or directly under the influence of TC-ICS (spec pg 11) which apparently covers most every effect known to be related to ion transporters.

The problem is further confounded by the requirement that the "functional effect is under the influence of the TC-ICS". The specification apparently mischaracterizes the functional activity of the TC-ICS. At page 54, the specification asserts that modulation of taste

transduction is assayed by measuring changes in intracellular Ca^{2+} levels, which change in response to modulation of the TC-ICS signal transduction pathway via administration of a molecule that associates with TC-ICS. No actual functional data is provided for the TC-ICS, and presumably these assertions are based on the speculation that the TC-ICS has the properties of other known TRP channel family members, e.g. see page 53. TRP channels are known to be Ca^{2+} channels that increase intracellular Ca^{2+} levels by bringing in Ca^{2+} through the plasma membrane. However the instant TC-ICS (Trpm5) is known to be unique among Trp proteins in that it is impermeable to Ca^{2+} and is instead activated by intracellular Ca^{2+}. Activation then leads to a nonspecific monovalent ion influx, reviewed by Ullrich-ND et al., Cell Calcium 37(267-278)2005. Thus activation of TC-ICS is not the *cause* of changes in intracellular Ca^{2+}, rather activation appears to be the *result* of changes in intracellular Ca^{2+}. Thus, one skilled in the art would not understand *which ion* the claims refer to in the phrases "a change in intracellular ion concentration" or "a change in transmembrane ion flux of an ion", or *which change* the claims refer to in the phrase "a change in intracellular Ca^{2+}" that is "under the influence of the TC-ICS".

Furthermore, the phrase "or a change in intracellular Ca^{2+}" is indefinite, alone, because it does not set forth *what* is actually changing with regard to "intracellular Ca^{2+}", e.g. concentration, localization, isotopic composition? Thus the phrase appears to be incomplete and the artisan could not be sure if he or she were actually practicing the claimed invention.

It is believed that the above discussion addresses Applicant's arguments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-9, 12, 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification proposes that at least one of SEQ ID NO: 2, 5, and 8 are taste receptor channels that modulate taste perception. Also proposed are a multitude of assays, used in the art to study particular biochemical pathways involved with different aspects taste signal transduction as well as signal transduction in general, see pages 23-28. Yet in order to practice the invention as claimed, one skilled in the art would need to know which of these assays and which materials, could be used in conjunction with the polypeptide of SEQ ID NO: 8. The specification admits that it is well recognized in the art that the signal transduction schemes underlying taste transduction are bewilderingly complex and poorly understood, page 3. Thus, at best, at the time of filing one of skill in the art would expect that to carry out an extensive research plan to try to use the invention as claimed, if that can be done, would be unduly burdensome.

As discussed above, The specification apparently mischaracterizes the functional activity of the TC-ICS. At page 54, the specification asserts that modulation of taste transduction is assayed by measuring changes in intracellular Ca^{2+} levels, which change in response to modulation of the TC-ICS signal transduction pathway via administration of a molecule that associates with TC-ICS. No actual functional data is provided for the TC-ICS, and presumably

these assertions are based on the speculation that the TC-ICS has the properties of other known TRP channel family members, e.g. see page 53. TRP channels are known to be Ca^{2+} channels that increase intracellular Ca^{2+} levels by bringing in Ca^{2+} through the plasma membrane. However the instant TC-ICS (Trpm5) is known to be unique among Trp proteins in that it is impermeable to Ca^{2+} and is instead activated by intracellular Ca^{2+}. Activation then leads to a nonspecific monovalent ion influx; reviewed by Ullrich-ND et al., Cell Calcium 37(267-278)2005. Thus activation of TC-ICS is not the *cause* of changes in intracellular Ca^{2+}, rather activation appears to be the *result* of changes in intracellular Ca^{2+}. Thus, one skilled in the art would, presumably, wrongly attribute changes in intracellular Ca^{2+} concentration, localization, etc. or to changes in transmembrane ion flux, to effects of the compound on the TC-ICS and would thus not be practicing the invention as claimed, i.e. detecting a functional effect of a compound on a cell or cell membrane wherein the functional effect was not "under the influence of the TC-ICS".

Furthermore, claims 12, 14-15 require compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8. There is no teaching of compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8 and one of skill in the art would view the invitation to randomly sample chemicals in the hope of finding such would be unduly burdensome. Nor does the specification provide assays adequate to identify such compounds, as discussed above. It is believed that the discussion above has addressed Applicant's arguments.

Claims 1, 4-9, 12, 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification proposes that at least on of SEQ ID NO: 2, 5, and 8 are taste receptors that modulate taste perception. Also proposed are a multitude of assays, used in the art to study particular biochemical pathways involved with different aspects taste signal transduction as well as signal transduction in general, see pages 23-28. Yet in order to practice the invention as claimed, one skilled in the art would need to know which of these assays and which materials, could be used in conjunction with the polypeptide of SEQ ID NO: 8. The specification admits that it is well recognized in the art that the signal transduction schemes underlying taste transduction are bewilderingly complex and poorly understood, page 3. In fact, it appears that the specification apparently mischaracterizes the functional activity of the TC-ICS. At page 54, the specification asserts that modulation of taste transduction is assayed by measuring changes in intracellular Ca^{2+} levels, which change in response to modulation of the TC-ICS signal transduction pathway via administration of a molecule that associates with TC-ICS. No actual functional data is provided for the TC-ICS, and presumably these assertions are based on the speculation that the TC-ICS has the properties of other known TRP channel family members, e.g. see page 53. TRP channels are known to be Ca^{2+} channels that increase intracellular Ca^{2+} levels by bringing in Ca^{2+} through the plasma membrane. However the instant TC-ICS (Trpm5) is known to be unique among Trp proteins in that it is impermeable to Ca^{2+} and is instead activated by intracellular Ca^{2+}. Activation then leads to a nonspecific monovalent ion influx; reviewed by Ullrich-ND et al., Cell Calcium 37(267-278)2005. Thus activation of TC-ICS is not the *cause* of changes in intracellular Ca^{2+}, rather activation appears to be the *result* of

changes in intracellular Ca^{2+}. Thus, one skilled in the art would, presumably, wrongly attribute changes in intracellular Ca^{2+} concentration, localization, etc. or to changes in transmembrane ion flux, to effects of the compound on the TC-ICS and would thus not be practicing the invention as claimed, i.e. detecting a functional effect of a compound on a cell or cell membrane wherein the functional effect was not "under the influence of the TC-ICS". Thus, one of skill in the art would not recognize that Applicant was in possession of methods that require determining a functional effect of a compound on a cell or cell membrane expressing a TC-ICS wherein the functional effect is under the influences of the TC-ICS.

Furthermore, claims 12, 14-15 require compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8. There is no teaching of compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8 and one of skill in the art would view the invitation to randomly sample chemicals in the hope of finding such would be unduly burdensome. Nor does the specification provide assays adequate to identify such compounds, as discussed above. It is believed that the discussion above has addressed Applicant's arguments. Thus, one skilled in the art would not recognize that applicant was in possession of the claimed methods because the required compounds are neither taught explicitly nor are methods for attaining them adequately described.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4-9, 12, 14-17 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Publication 20020037515, published March 28, 2002, which is fully supported by prior provisional application, US 60/197491, filed April 17, 2000.

Clarification of the record is required. It was previously asserted that the TRP8 polypeptide of 20020037515-5 was identical to the instant TC-ICS (SEQ ID NO: 8) with the two exceptions that the glutamine at position 630 is missing in TRP8 and threonine is substituted for Aspartic acid at position 990. However, this appears to be a consequence of an error in the electronic form of the sequence listing in the application corresponding to the 20020037515 publication. The amino acid sequence of the TRP8 polypeptide of 20020037515-5 is disclosed in the prior US 60/197491 application in Fig 4 and is identical to the instant SEQ ID NO: 8.

Claims 1, 4-9, 12, 14-17 of the instant application are unpatentable over claims 17, 18 and 21 of US Patent Publication 20020037515, as set forth an annotated below.

17. A method for identifying a compound that induces the perception of a bitter taste (*e.g. modulates taste signaling in taste cells*) comprising: (i) contacting a cell expressing

the TRP8 channel protein (*identical to the SEQ ID NO: 8*) with a test compound and measuring the level of TRP8 activation; (ii) in a separate experiment, contacting a cell expressing the TRP8 channel protein with a vehicle control and measuring the level of TRP8 activation where the conditions are essentially the same as in part (i); and (iii) comparing the level of activation of TRP8 measured in part (i) with the level of activation of TRP8 in part (ii), wherein an increased level of activated TRP8 in the presence of the test compound indicates that the test compound is a TRP8 inducer. (*Measuring the level of TRP8 activation is essentially equivalent to detecting a functional effect of the compound, wherein the functional effect is under the influence of the TS-ISC of SEQ ID NO: 8*).

18. A method for identifying a compound that inhibits the perception of a bitter taste and/or promotes the perception of a sweet taste comprising: (i) contacting a cell expressing the TRP8 channel protein with a test compound in the presence of a bitter tastant and measuring the level of TRP8 activation; (ii) in a separate experiment, contacting a cell expressing the TRP8 channel protein with a bitter tastant and measuring the level of TRP8 activation, where the conditions are essentially the same as in part (i); and (iii) comparing the level of activation of TRP8 measured in part (i) with the level of activation of TRP8 in part (ii), wherein a decrease level of activation of TRP8 in the presence of the test compound indicates that the test compound is a TRP8 inhibitor.

21. A method of inhibiting a bitter taste resulting from contacting a taste tissue of a subject with a bitter tastant, comprising administering to the subject an effective amount of a bitterness inhibitor (*e.g. a compound identified by the method of claim 18*).

US Patent Publication 20020037515 discloses that TRP8 activation can be measured as changes in membrane potential, i.e. a change in transmembrane ion flux, see [0059] and that the recombinant TRP8 protein can be expressed in HEK-293 cells, see [0059].

Applicant argues that the Zuker Declaration establishes priority of invention before the priority date of the 20020037515 publication. This argument has been fully considered but not deemed persuasive. The 20020037515 reference is a U.S. patent application publication of a pending or patented application that claims the rejected invention. An affidavit or declaration is inappropriate under 37 CFR 1.131(a) when the reference is claiming the same patentable invention, see MPEP § 2306. If the reference and this application are not commonly owned, the reference can only be overcome by establishing priority of invention through interference proceedings. See MPEP Chapter 2300 for information on initiating interference proceedings. If the reference and this application are commonly owned, the reference may be disqualified as prior art by an affidavit or declaration under 37 CFR 1.130. See MPEP § 718.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 12, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER